

Off-the-shelf cell therapy with induced pluripotent stem cell-derived natural killer cells.

Journal:	Semin Immunopathol
Publication Year:	2019
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PubMed link:	30361801
Funding Grants:	Targeted off-the-shelf immunotherapy to treat refractory cancers, Human Embryonic Stem Cell-Derived Natural Killer Cells for Cancer Treatment

Public Summary:

Cancer immunotherapy is a therapy used to treat cancer patients that uses agents that stimulate or suppress components of their own immune system. There are several types of immunotherapies, including monoclonal antibodies, cancer vaccines, T-cell therapy etc. Monoclonal antibodies can bind to, and inhibit the function of, proteins expressed by cancer cells. Another approach, called adoptive cell transfer, uses certain white blood cells that fight cancer – these cells can be collected from the patients' own immune system (autologous) or from related or unrelated donors (allogeneic). Cells are typically activated or genetically modified in a laboratory to enhance their anti-tumor activity. Cell therapy is emerging as a very promising therapeutic modality against cancer, spearheaded by the clinical success of chimeric antigen receptor (CAR) modified T cells for B cell malignancies. Currently, FDA-approved CAR-T cell products are based on engineering of autologous T cells harvested from the patient, typically using a central manufacturing facility for gene editing before the product can be delivered to the clinic and infused to the patients. For a broader implementation of advanced cell therapy and to reduce costs, it would be advantageous to use allogeneic "universal" cell therapy products that can be stored in cell banks and provided upon request, in a manner analogous to biopharmaceutical drug products. In this review, we outline a roadmap for development of off-the-shelf cell therapy based on natural killer (NK) cells derived from induced pluripotent stem cells (iPSCs). We discuss strategies to engineer iPSC-derived NK (iPSC-NK) cells for enhanced functional potential, persistence, and homing.

Scientific Abstract:

Cell therapy is emerging as a very promising therapeutic modality against cancer, spearheaded by the clinical success of chimeric antigen receptor (CAR) modified T cells for B cell malignancies. Currently, FDA-approved CAR-T cell products are based on engineering of autologous T cells harvested from the patient, typically using a central manufacturing facility for gene editing before the product can be delivered to the clinic and infused to the patients. For a broader implementation of advanced cell therapy and to reduce costs, it would be advantageous to use allogeneic "universal" cell therapy products that can be stored in cell banks and provided upon request, in a manner analogous to biopharmaceutical drug products. In this review, we outline a roadmap for development of off-the-shelf cell therapy based on natural killer (NK) cells derived from induced pluripotent stem cells (iPSCs). We discuss strategies to engineer iPSC-derived NK (iPSC-NK) cells for enhanced functional potential, persistence, and homing.

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